

Original Research Article

Evaluation of visual evoked potentials in type II diabetes mellitus subjects attending a tertiary care hospital

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ABSTRACT

Background: DM is the most common metabolic disorder in the world. The complications of DM take millions of lives every year. There is definite expectation to reason out both vasculopathy and neuropathy associated with DM leads to dysfunction along the visual pathway. The Visual Evoked Potentials (VEPs) as an electrophysiological method to assess conduction in type II DM subjects which is simple. This study attempted to detect earlier visual involvement before the clinical symptoms.

Methods: VEP was recorded in 100 subjects (Diabetic 50 and Controls 50) P100 latency was compared between the diabetic and age, gender matched controls.

Results: The study evidenced that the mean P 100 latency in DM subjects was found to be significantly prolonged when compared the that of controls.

Conclusions: The study will help in supervising the earlier progress of neuropathy and earlier detection of nervous system involvement to reduce the morbidity of the diabetic subject and a special care to improve their quality of life.

Keywords: Neuropathy, P 100 latency, Type II diabetes mellitus, Visual evoked potentials

INTRODUCTION

The term diabetes which means to pass through was first used by the Roman Physician Aretaeus in the 2nd century A.D. There was a dawn to human sufferings by the seminal work of Banting et al in 1921 to isolate the exact substance secreted by the pancreas that prevented the development of diabetes initially named isletin, then was later rechristened insulin. The developments of the last 150 years in medicine have made a dramatic difference to the life of a person with diabetes. Patients with type II diabetes mellitus (DM) can now expect to live longer and more comfortably than they ever did in the past. The recent modalities of treatment do not exactly restore normoglycemia in a physiologic manner and are not

totally devoid of side effects, either. The complications of DM take millions of lives every year.

Defining about the disease- diabetes mellitus (DM) describes a metabolic cum vascular syndrome of multiple etiology singly characterized by chronic hyperglycemia with disturbances of all metabolisms resulting from defects in insulin secretion, insulin action, or both leading to changes in both small blood vessels (microangiopathy) and large blood vessels (macroangiopathy).

DM is the most common metabolic disorder in the world. According to International Diabetes Federation 2015, 415 million people in the world live with diabetes as of 2015 and 438 million people will be affected by DM in the year 2030.¹ In India, the prevalence rate of DM have

increased dramatically since the year 1971, when national level surveys conducted. It was 2.3% in urban and 1.2% in rural areas. Recently increased to 15-20% in urban and about (half) 50% of that in rural areas. The increasing prosperity and urbanization have led to changes in lifestyle causing DM in individuals who have a genetic predisposition to the disease. India is in the phase of explosion of type II DM.

Recent studies show that more than 50% of individuals with diabetes who had poor control of blood glucose and that essential tests like Hb A1C were being routinely done and awareness to be improved to the patient as well as health care system.

Type II DM represents a continuum of clinical scenarios ranging from severe insulin resistance with relative insulin deficiency of varying degrees. Defective insulin action in the liver leads to inappropriate release of glucose leading to hyperglycemia. DM comprises a spectral array of metabolic disorders that have commonly the phenotype of hyperglycemia. It leads to neurotransmitters dysfunction. DM is proinflammatory state where levels of inflammatory markers like C reactive protein, TNF α are found to be elevated.

There is definite expectation to reason out both vasculopathy and neuropathy associated with DM leads to dysfunction along the visual pathway.² After 15 years of DM, approximately 2% of people become blind, and about 10% develop severe visual impairment.³ The involvement of central nervous system in DM is recent concept. Woltman and Wilder concluded from pathological material that diabetic neuropathy is a disease of peripheral nerves and that degeneration in the CNS is unimportant. However, it is reasonable to ask whether such an ubiquitous metabolic derangement and diffuse angiopathy might involve any part of the nervous system. Recent studies showed the involvement of brain parenchyma in patients with long standing diabetes mellitus.⁴ The central nervous system could also be abnormal in diabetic patients.⁵⁻⁷

The neurophysiological studies of the CNS in diabetic patients involves measurements of evoked potential latencies. Increases in the latencies of evoked potentials of different modalities, including visual evoked potentials (VEPs), brainstem auditory evoked potentials (BAEPs) and somatosensory evoked potentials, have often been reported.⁸

METHODS

The main aim of the study is to evaluate conduction in optic pathway of Type II DM subjects to compare with normal healthy controls. The objectives are to use the Visual Evoked Potentials as an electrophysiological method to assess conduction in Type II DM subjects. Ethical Clearance obtained from Institutional Ethics Committee.

The Study group was 50 Type II diabetes mellitus subjects selected from Diabetic OP Department. The Control group was age and gender matched healthy subjects with normal fasting and postprandial blood sugar from the Master Health Check Up.

Inclusion criteria

- Age group 40 - 50 years, of both gender
- Type II diabetic patients with or without symptoms of neuropathy
- Both recently diagnosed and chronic diabetic patients
- Patients on oral hypoglycemic agents or insulin or both
- Visual acuity checked with Snellen's chart and ophthalmological examination were done to rule out any visual disorder.

Exclusion criteria

- Corneal opacity, squint, cataract, glaucoma, maculopathy
- Use of miotic or mydriatic drugs
- Refractive errors
- Systemic diseases like hypothyroidism, hypertension, chronic associated disorders such as cardiac decompensation, renal disorders, other demyelinating neuromuscular disorders
- Drugs acting on central nervous system
- Patients on drugs leading to neuropathy
- Patients with cochlear implant / cardiac pacemakers
- Habitual history of smoking and alcohol drinking,
- History of head injury.

The detailed procedure and purpose of the study was explained in the regional language. The written informed consent was taken from each subject in regional language before they entered the study. The participants were made to relax and to be comfortable prior to the test. A detailed clinical history about Type II diabetes mellitus is collected and thorough physical examination was performed. The basic parameters such as height, weight, pulse rate including body temperature were recorded. The blood investigations and other reports were noted in a pre-structured proforma. The subjects were properly instructed and motivated to provide full cooperation and selected by simple random sampling method.

VEP recording is done using Neuro Perfect Plus Medicaid POLYRITE, Solokraft industries, Chandigarh, India was used in Electrophysiology laboratory.

The study group were instructed to have shampoo head bath and avoid oil on hair or hair spray with removal of metal ornaments. The subjects were instructed to avoid beverages or strenuous exercises on the day of recording. The room was made quiet and comfort and uniform temperature maintained. The subject should be grounded properly. The skin and the electrode, electrical impedance

was checked. The usual spectacles (if any), were allowed to wear during the test. Automatic artefact rejection was used. Electrical activity has low cut of 2 Hertz and high cut of 0.3 Kilo Hertz filters. Disc surface electrodes were used. Sweep speed was 50 ms/division. Mono ocular stimulation was chosen with flash checker board.

The checker board stimulus was produced by a video pattern generator on a computer monitor provided with the polyrite, with black and white checks that changed phase (i.e., black to white and white to black) abruptly and repeatedly. Luminance modulation of the pattern was selected to give the reversal mode of stimulation at a rate of 2 per second. The check size was 8×8 and the monitor 16'× 14'. The luminances of bright and dark checks were adjusted to be 80%. The black and white monitor was placed 100 cm from the study subjects. Gold plated copper disc electrodes placed with electrode paste after cleansing the skin with spirit and cleansing gel.

The 10 - 20 international system of electrode placement was followed to ensure the reproducible electrode placement in the serial recordings. Reference- Cz 15 cm from bridge of nose to vertex, Active- Oz 5 cm above the inion and Ground- Fpz at middle of forehead. Responses to 100 stimuli were averaged. The signals were amplified, averaged and displayed on the monitor as a waveform. The signal is amplified 50,000 times and band pass filtered between 0.1-100 Hz.

Two averages were obtained under each stimulus condition to check for consistency, and quantitative analysis was performed on the average of these two. The study subjects were given short periods of rest between each separate measurement so as to minimize fatigue and any concomitant increase in response variability.⁹

With respect to latency, P 100 component was analyzed. Permanent records of the responses were made. The subjects were being instructed to fix their gaze at the centre of the checker board, a red square to avoid interference in potentials due to movement of eyeball. Prior to commencement of the test, the subject is pre-adapted to the luminance of the blank screen for five minutes.

This was the only source of illumination in an otherwise darkened room. The other eye is covered with opaque

material that does not allow light. The function of the central visual pathway was evaluated by pattern VEP. All techniques of measurement and instruments were maintained uniformly throughout the study including the laboratory temperature.^{10,11}

The responses of VEPs from the left and right eyes as, N 75, P 100*, N 145, P 100 - N 75 were noted from the waveform recordings. VEPs consist of a series of waveforms of opposite polarity, a negative waveform (denoted as N) and a positive waveform (denoted as P); which is followed by the approximate latency in milliseconds (Table 2). In VEP, the wave latency P100 which is the most significant parameter is measured from the waveforms recorded.

Analysis of VEP parameters may provide earlier diagnosis of diabetic changes and determine prognosis during treatment.¹² VEP can detect any defects from the pathway from the optic nerve to the visual calcarine cortex.¹³ There have been reports from Western countries showing alterations in visual stimuli evoked potential wave latencies in diabetic patients.¹⁴

RESULTS

All the data were expressed as mean±SD. The study group consists of 50 Type II DM subjects and 50 healthy controls. The mean age was 45.00±3 as detailed in Table 1. There was no statistical difference between Type II DM subjects group and controls with regards to age and BMI. Visual evoked potentials of both the eyes were tested. The negative and positive wave latencies were measured. The parameter for the study was Peak P 100 latency which was considered the important cortical wave latency. Results were analysed by student's independent t- test using Statistical Package for Social Sciences 11.5 version. P value was calculated to test the statistical significance. The level of significance chosen for the study was 1% (p < 0.01).

Interpretation

There is considerable prolongation of the important Peak latency P 100 in Type II DM subjects which is statistically significant.

Table 1: Anthropometric measurements of type II DM subjects and controls.

Anthropometric measurements	Type II DM subjects (n = 500) Mean±SD	Controls (n = 50) Mean±SD	P value
Age (years)	45.00±3.56	45.00±2.89	0.15
Height (cm)	158.80±10.24	153.17±8.64	0.13
Weight (Kgs)	68.13±11.81	60.87±9.73	0.12
BMI (Kg/m ²)	27.24±2.22	25.63±2.85	0.06

BMI = Body mass Index; * P <0.05 is significant

Table 2: P 100 Wave Latency of Type II DM subjects compared with controls.

VEP Response P 100 Latency	Type II DM subjects (n = 50) Mean±SD	Controls (n = 50) Mean±SD	P value
Left eye	107.77±3.62	105.45±4.75	0.03*
Right eye	108.85±3.61	106.14±4.28	0.01*

*P value <0.05 is significant.

DISCUSSION

VEP is a very simple, sensitive, noninvasive and objective electrophysiologic technique for evaluating impulse conduction along the optic pathway (central nervous system). The present study deals with the abnormalities in VEP in non-insulin dependent diabetes mellitus subjects. The latency depends on an intact, myelinated nerve as myelin and the saltatory conduction are essential for fast action potential propagation in normal subjects. In contrast, the amplitude of the waveform depends primarily on number of axons functioning within the nerve. Slowing of conduction velocity or prolongation of latency usually implies demyelinating injury, while loss of amplitude usually correlates with axonal loss or dysfunction.¹⁵ Algan et al, reported prolonged P 100 latency in 50 DM patients, six of whom had diabetic retinopathy.¹⁶ In 19 patients with type II DM, they showed an increase in P 100 latency. Mariani et al, reported prolongation of P 100 latency in 35 diabetic patients who do not have retinopathy.¹⁷ Ponte et al, reported prolongation of PVEP latencies in 50 asymptomatic insulin dependent diabetic patients without retinopathy.¹⁸

Peripheral nerve impairment in DM and its relation to duration of disease and glycemic control have been well established both clinically and evidence-based research works. The involvement of the visual path deviations in DM as a part of Central nervous system (CNS) can very well announce the wide world the knowledge of electrophysiological findings of DM on CNS. Any hour before the onset of microvascular lesions in diabetic retinopathy, the neural retina if DM subjects eyes undergoes minimal changes not found by fundus photography.¹⁹

In the present study, the mean P 100 latency in DM subjects was found to be significantly prolonged when compared the that of controls (Table 2). the above said finding is in accordance with the similar studies in the past.

The exact pathophysiology of the central nervous dysfunction is not clear, but it seems to be multifactorial, involving metabolic and vascular factors, which is similar to the pathogenesis of diabetic peripheral neuropathy. The P100 wave form is generated in the striate and peristriate occipital cortex due to the activation of the primary visual cortex and also due to the discharge of the

thalamocortical fibers. The P100 is a prominent peak that shows relatively little variation between the subjects, minimal within interocular difference, and minimal variation with repeated measurements over time.²⁰ Therefore, the present study focused more on the correlation P100 latency values among the study groups which were examined.

Diabetic neuropathy has been called the silent complication of DM since people with severe neuropathy often have no symptoms referable to it. The two major features contributing to pathology of human diabetic neuropathy are nerve fibres degeneration and gross disease of the blood vessels supplying them. Microangiopathy is probably the main cause underlying the pathogenesis. The basic pathology may be progressive narrowing and occlusion of vascular lumina, impaired perfusion, ischemia and tissue damage. The tissue involved are endothelial cells, pericytes, Muller cells and ganglion cells of retina with myelinating cells of optic nerve too. The chronic complications due to hyperglycemia due to polyol pathway, advanced glycosylation end products, protein kinase C and hexosaminase path. Neuropoietic cytokines including interleukin- 1 (IL- 1), IL- 6, leukaemia inhibitory factor (LIF), ciliary neuro- trophic factor (CNTF), tumour necrosis factor alpha (TNF-alpha), and transforming growth factor- beta (TGF-beta), exhibit pleiotropic effects on the homeostasis of the glia and on the neurons in the central, peripheral, and the autonomic nervous systems.²¹

The study has to correlate parameters well with the duration of disease. A follow up study is needed to record VEP after the subjects get good glycemic status too.

CONCLUSION

It can be concluded that the central neuropathy (visual pathway) is involved in Type II diabetes mellitus as evidenced by an abnormal cortical VEP latencies i.e. P 100. This shows that there may be progressive demyelination occurring along with axonal loss or dysfunction in DM. Hence, this study suggests that periodic evaluation of diabetic individuals to such electrophysiological test will help in supervising the earlier progress of neuropathy and earlier detection of nervous system involvement to reduce the morbidity of the diabetic subject and a special care to improve their quality of life.

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